

CLAIMS

1. A method for producing a therapeutic effect, comprising:
administering to a pulmonary tissue of a subject an unformulated dry
5 polysaccharide particle in an effective amount for producing a therapeutic effect,
wherein the unformulated dry polysaccharide particle has a mean geometric diameter of
1-500 microns.
2. The method of claim 1, wherein the polysaccharide is a glycosaminoglycan.
- 10 3. The method of claim 2, wherein the glycosaminoglycan is a heparin.
4. The method of claim 2, wherein the glycosaminoglycan is a heparin sulfate.
- 15 5. The method of claim 2, wherein the glycosaminoglycan is a low molecular
weight heparin.
6. The method of claim 3, wherein the heparin is a biotechnology derived
heparin.
- 20 7. The method of claim 3, wherein the heparin is a chemically modified heparin.
8. The method of claim 2, wherein the glycosaminoglycan is a heparin analogue.
- 25 9. The method of claim 8, wherein the heparin analogue is selected from the
group consisting of an oligosaccharide and an AT-III binding pentasaccharide.
10. The method of claim 2, wherein the glycosaminoglycan is an unfractionated
heparin preparation.
- 30 11. The method of claim 1, wherein the unformulated dry polysaccharide particle
has a mean geometric diameter of 1-200 microns.

12. The method of claim 1, wherein the unformulated dry polysaccharide particle has a mean geometric diameter of 1-53 microns.

5 13. The method of claim 1, wherein the unformulated dry polysaccharide particle has a mean geometric diameter of 53-106 microns.

14. The method of claim 1, wherein the unformulated dry polysaccharide particle has a mean geometric diameter of 1-5 microns.

10

15. The method of claim 1, wherein the unformulated dry polysaccharide particle has a mean aerodynamic diameter of 1-5 microns.

16. The method of claim 1, wherein the unformulated dry polysaccharide particle has a mean aerodynamic diameter selected from the group consisting of 5-35 and 35-75 microns.

15

17. The method of claim 2, wherein the subject has or is at risk of a coagulation disorder and the therapeutic effect of the glycosaminoglycan is anti-coagulation or antithrombosis.

20

18. The method of claim ~~17~~, wherein the coagulation disorder is selected from the group consisting of thrombosis associated with cardiovascular disease and vascular conditions.

25

19. The method of claim 18, wherein the cardiovascular disease is selected from the group consisting of acute myocardial infarction, unstable angina, and atrial fibrillation.

30

20. The method of claim 18, wherein the vascular condition is selected from the group consisting of deep venous thrombosis, stroke, and pulmonary embolism.

5 22. The method of claim 2, ~~wherein~~ wherein the subject is preparing to undergo, is undergoing or is recovering from a surgical procedure.

24. The method of claim 2, wherein the subject has or is at risk of atherosclerosis.

15 25. The method of claim 2, wherein the subject has or is at risk of a respiratory disorder.

26. The method of claim 25, wherein the respiratory disorder is selected from the group consisting of asthma, emphysema, adult respiratory distress syndrome (ARDS), and lung reperfusion injury.

27. The method of claim 2, wherein the subject has or is at risk of developing a cancer or metastasis.

25 28. The method of claim 2, wherein the subject has or is at risk of developing an
inflammatory disorder.

29. The method of claim 2, wherein the subject has or is at risk of developing an allergy.

30. The method of claim 2, wherein the subject has or is at risk of developing an angiogenic disorder and the glycosaminoglycan is administered in an effective amount for preventing angiogenesis.

5 31. The method of claim 2, wherein the angiogenic disorder is selected from the group consisting of neovascular disorders of the eye, osteoporosis, psoriasis, and arthritis.

10 32. The method of claim 1, wherein the polysaccharide is selected from the group consisting of chondroitin sulfate, dermatan sulfate, hyaluronic acid, Pectin, pectin derivatives, oligosaccharides and pentasaccharides that bind to AT-III.

15 33. The method of claim 1, wherein the unformulated dry polysaccharide is self administered by the subject.

 34. The method of claim 1, wherein the unformulated dry polysaccharide is administered through a tracheal tube.

20 35. The method of claim 2, wherein the subject is undergoing a tissue or organ transplant.

 36. The method of claim 1, wherein the unformulated dry polysaccharide has a tap density of 0.01 - 0.4 g/cm³.

25 37. The method of claim 1, wherein the unformulated dry polysaccharide has a tap density of greater than 0.4 g/cm³.

 38. A method for delivering at least 5% of a polysaccharide to lower respiratory tract, comprising:

30 administering to a pulmonary tissue of a subject an unformulated dry polysaccharide particle, wherein the unformulated dry polysaccharide particle has a

mean geometric diameter of 1-500 microns, and wherein at least 5% of the polysaccharide administered is delivered to the lower respiratory tract.

39. The method of claim 38, wherein at least 10% of the polysaccharide administered is delivered to the lower respiratory tract.

40. The method of claim 38, wherein at least 30% of the polysaccharide administered is delivered to the lower respiratory tract.

41. The method of claim 38, wherein at least 50% of the polysaccharide administered is delivered to the lower respiratory tract.

42. A method for systemically delivering a polysaccharide to a subject, comprising:

administering to a pulmonary tissue of the subject an unformulated dry polysaccharide particle, wherein the unformulated dry polysaccharide particle has a mean geometric diameter of 1-500 microns.

43. A composition consisting of unformulated dry glycosaminoglycan having a mean geometric diameter of 1-500 microns.

44. The composition of claim 43, wherein the unformulated dry glycosaminoglycan has a mean geometric diameter of 1-200 microns.

45. The composition of claim 43, wherein the unformulated dry glycosaminoglycan has a mean geometric diameter of 1-53 microns.

46. The composition of claim 43, wherein the unformulated dry glycosaminoglycan has a mean geometric diameter of 1-5 microns.

47. The composition of claim 43, wherein the unformulated dry glycosaminoglycan has a mean geometric diameter of 5-53 microns.

48. The composition of claim 43, wherein the unformulated dry

49. The composition of claim 43, wherein the glycosaminoglycan is selected from the group consisting of a heparin, a heparin sulfate, a low molecular weight heparin, a biotechnology derived heparin, a chemically modified heparin, a heparin analogue, and an unfractionated heparin preparation.

10 50. The composition of claim 43, further comprising a formulated dry
glycosaminoglycan preparation

51. The composition of claim 50, wherein the glycosaminoglycan of the formulated dry glycosaminoglycan preparation is selected from the group consisting of a heparin, a heparin sulfate, a low molecular weight heparin, a biotechnology derived heparin, a chemically modified heparin, a heparin analogue, and an unfractionated heparin preparation.

52. The composition of claim 50, wherein the glycosaminoglycan of the
20 formulated dry glycosaminoglycan preparation is the same as the glycosaminoglycan of
the unformulated dry glycosaminoglycan preparation

53. The composition of claim 50, wherein the glycosaminoglycan of the formulated dry glycosaminoglycan preparation is different than the glycosaminoglycan of the unformulated dry glycosaminoglycan preparation.

54. The composition of claim 50, wherein the formulated dry glycosaminoglycan preparation includes a polymer to effect slow release of the glycosaminoglycan

30 55. The composition of claim 54, wherein the polymer is selected from the group
consisting of PLA, PGA, and PLGA.

56. The composition of claim 50, wherein the formulated dry glycosaminoglycan preparation includes a surfactant.

57. The composition of claim 56, wherein the surfactant is DPPC.

58. A method for delivering a glycosaminoglycan to a subject, comprising, administering to a pulmonary tissue of a subject the composition of any one of claims 43-57.

10 59. A method of rapidly delivering a polysaccharide to a subject comprising: administering a dry aerosol containing a polysaccharide to a pulmonary tissue of a subject in an effective amount to produce a peak plasma concentration of polysaccharide within two hours.

15 60. The method of claim 59, wherein dry aerosol containing a polysaccharide is administered in an effective amount to produce the peak concentration or activity of polysaccharide within one and one half hours.

20 61. The method of claim 59, wherein dry aerosol containing a polysaccharide is administered in an effective amount to produce the peak concentration or activity of polysaccharide within one hour.

25 62. The method of claim 59, wherein dry aerosol containing a polysaccharide is administered in an effective amount to produce the peak concentration or activity of polysaccharide within one half hour.

63. The method of claim 59, wherein the polysaccharide is a glycosaminoglycan.

30 64. The method of claim 63, wherein the glycosaminoglycan is selected from the group consisting of a low-molecular-weight heparin, heparin, heparin sulfate, biotechnology derived heparin, chemically modified heparin, heparin analogue, and unfractionated heparin preparation.

65. The method of claim 59, wherein the dry aerosol contains an unformulated dry polysaccharide.

5 66. The method of claim 59, wherein the dry aerosol contains a dry polysaccharide formulated in a surfactant.

67. The method of claim 66, wherein the surfactant is DPPC.

10 68. The method of claim 66, wherein the surfactant is coated on the particle surface.

69. The method of claim 66, wherein the surfactant is incorporated into the formulation.

15 70. The method of claim 59 further comprising administering an additional therapeutic agent.

20 71. The method of claim 70, wherein the additional therapeutic agent is selected from the group consisting of proteins, peptides, nucleic acids, and small organic molecules.

25 72. The method of claim 59, wherein the dry aerosol containing a polysaccharide includes both a formulated and an unformulated dry polysaccharide.

73. A method of rapidly delivering a polysaccharide to a subject comprising:
administering a dry aerosol containing a polysaccharide to a pulmonary tissue of
a subject in an effective amount to deliver at least 5% of the polysaccharide to the blood
within one hour.

30 74. A method of claim 73, wherein at least 10% of the polysaccharide is delivered to the blood within one hour.

75. The method of claim 73, wherein at least 20% of the polysaccharide is delivered to the blood within one hour.

5 76. The method of claim 73, wherein at least 40% of the polysaccharide is delivered to the blood within one hour.

77. The method of claim 73, wherein at least 50% of the polysaccharide is delivered to the blood within one hour.

10 78. A method of claim 73, wherein at least 10% of the polysaccharide is detectable in the blood within one hour.

✓ 79. A method for producing a rapid therapeutic effect, comprising:
15 administering a dry aerosol containing a polysaccharide to a pulmonary tissue of a subject in an effective amount for producing a therapeutic effect within 1 hour of administration.

80. The method of 79, wherein the dry aerosol is administered in an effective
20 amount for producing a therapeutic effect within 15 minutes of administration.

81. The method of 79, wherein the dry aerosol is administered in an effective amount for producing a therapeutic effect within 10 minutes of administration.

✓ 82. A composition comprising a dry aerosol formulation of particles containing a
25 heparin-like glycosaminoglycan, wherein the particles have a mean geometric diameter of greater than 30 microns.

83. The composition of claim 82, wherein the particles are spherical.

30 84. The composition of claim 82, wherein the particles are non-spherical.

Patented June 22, 1993

- 60 -

2, wherein the partic

, wherein the partic

, further comprising

, further comprising

lycan.

, further co

, further co

lycan.



✓

~~the polysacch
the glycosam
ght heparin, l
ly modified h~~

93. The kit of claim 92, wherein the glycosaminoglycan is selected from the group consisting of a low-molecular-weight heparin, heparin, heparin sulfate, biotechnology derived heparin, chemically modified heparin, heparin analogue and unfractionated heparin preparation.

94. The kit of claim 91, wherein the mean geometric diameter of the particles is between 1 and 500 μm .

95. The kit of claim 91, wherein the mean geometric diameter of the particles is between 1 and 106 μm .

96. The kit of claim 91, wherein the mean geometric diameter of the particles is between 5 and 53 μm .

97. The kit of claim 91, wherein the aerodynamic diameter of the particles is between 1 and 5 μm .

98. The kit of claim 91, wherein the aerodynamic diameter of the particles is selected from the group consisting of 5-35 and 35-75 microns..

99. A method for delivering a polysaccharide to a subject, comprising:
administering to a pulmonary tissue of the subject a dry aerosol formulation comprising an unformulated dry glycosaminoglycan preparation and a formulated dry glycosaminoglycan preparation to deliver the polysaccharide to the subject.

100. The method of claim 99, wherein the ratio of unformulated preparation to formulated preparation is 90:10.

101. The method of claim 99, wherein the ratio of unformulated preparation to formulated preparation is 70:30.

102. The method of claim 99, wherein the ratio of unformulated preparation to formulated preparation is 50:50.

103. The method of claim 99, wherein the ratio of unformulated preparation to formulated preparation is 30:70.

105. The method of claim 99, wherein the polysaccharide is a glycosaminoglycan and the glycosaminoglycan is selected from the group consisting of a heparin, a heparin sulfate, a low molecular weight heparin, a biotechnology derived heparin, a chemically modified heparin, a heparin analogue, and an unfractionated heparin preparation.

107. The method of claim 105, wherein the glycosaminoglycan of the formulated dry glycosaminoglycan preparation is different than the glycosaminoglycan of the unformulated dry glycosaminoglycan preparation.

108. The method of claim 99, wherein the formulated dry glycosaminoglycan preparation includes a polymer to effect slow release of the glycosaminoglycan.

109. The method of claim 108, wherein the polymer is selected from the group consisting of PLA, PGA, and PLGA.

110. The method of claim 99, wherein the formulated dry glycosaminoglycan preparation includes a surfactant.

111. The method of claim 110, wherein the surfactant is DPPC.

112. The method of claim 99, wherein the relative ratio of formulated to unformulated preparation is selected from the group consisting of 10:90, 20:80, 30:70, 40:60, 50:50, 60:40, 70:30, 80:20, and 90:10.